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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,504	12/19/2005	Julia Cianci	Q88025	6545

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SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
PESELEV, ELLI	
ART UNIT	**PAPER NUMBER**
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,504	CIANCI ET AL.	
	Examiner	Art Unit	
	Elli Peselev	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32,37-67 and 72* is/are pending in the application.

4a) Of the above claim(s) *2-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-32,37-67 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 2-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 12, 2007. Note that claims 2-5 are limited to the compound of formula (III) containing a pharmaceutically active moiety represented by the variable X'.

Applicant's election with traverse of species of structural formula (I) in the reply filed on November 12, 2007 is acknowledged.

Claims 1, 6-32, 37-67 and 72 have been examined only insofar as the elected species of structural formula (I) are concerned.

The abstract of the disclosure is objected to because it has not been presented in the proper domestic form. Correction is required. See MPEP § 608.01(b).

Claim 47 is objected to because of the following informalities: the term "substituted in line 5 is misspelled. Appropriate correction is required.

Claims 1, 6-32, 37 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tobramycin prodrugs having structural formulae as set forth in Tables 2-4 on pages 47-61 of the specification, does not reasonably provide enablement for any aminoglycoside, linker group and a pharmacokinetic regulator attached at any position on an aminoglycoside antibiotic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims.

The claims encompass an enormous number of possible prodrugs of any aminoglycosides.

(B) The state of the prior art.

Shechter et al (J. Med. Chem. 2002, 45, 4264-4270) disclose N-[2-sulfo0-9-fluorenylmethoxycarbonyl]3-gentamicin C1 prodrug.

(C) The level of predictability in the art.

The art of making specific prodrugs which have the desired properties and activity is highly unpredictable.

(D) The existence of working examples.

The working examples are limited to a number of specific tobramycin prodrugs set forth in Tables 2-4 of the specification.

(E) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Because there is no way to predict a priori which other prodrugs, besides those specifically disclosed, will produce an antibiotic having desired activity, it would take an enormous amount of trial and error to test various prodrugs encompassed by the present claims.

Claims 20, 21, 28-32, 55, 56 and 63-67 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of a bacterial infection with the combination of the claimed compound or the claimed compound in combination with an antibacterial agent, does not reasonably provide enablement for a method of the treatment or prevention of any microbial infection and for a composition comprising the claimed compound in combination with any therapeutic and/or prophylactic ingredients or any antimicrobial agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention.

(A) The breadth of the claims.

The broadest reasonable interpretation of the terms "prophylactic" and "prevention" merely requires that one microorganism gain entry into the cells of a host. There is no evidence that entry would be prevented. Therefore, the claims encompassing prophylactic agents and methods of prevention lack enablement.

The term "antimicrobial" encompasses all possible infection, including viral infections.

(B) The state of the prior art.

Aminoglycoside antibiotics are known antibacterial agents. The use of aminoglycosides for the treatment of viral infections is not known in the prior art.

(C) The existence of working examples.

The working examples are limited to showing that the claimed compounds possess antibacterial activity.

(D) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Because there is no way to predict a priori for the treatment of which other antimicrobial infections, besides, bacterial infections, in combination with which other therapeutic and/or prophylactic ingredients the claimed compositions and methods would be useful, it would take an undue amount of experimentation to test the claimed compounds alone or in combination with other ingredients against a large number of various antimicrobial infections, including antiviral infections.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-54, 63-67 and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakagawa et al (Microbial Drug Resistance, 176, 2, 269-272), Nakagawa et al (Journal of Antibiotics, 1978, 31(7), 675-680), , Shechter et al (J. Med. Chem. 2002, 45, 4264-4270), Umezawa et al (U.S. Patent No. 3,940,382), or Cron et al (U.S. Patent No. 4,347,354).

Nagawa et al (Microbial Drug Resistance) (page 269) and Nakagawa et al (J. of Antibiotics) (page 675) discloses the claimed compound kanamycin acylated with 4-amino0hydroxybutyric acid (page 269).

Shechter et al disclose the claimed compound N-[2-Sulfo)-9-fluoromethoxycarbonyl]3-gentamicin C1.

Umezawa et al disclose the claimed compound 1,2'-di-N-(hydroxy-aminoacyl) kanamycin B (column 1).

Cron et al disclose the claimed compounds 1-N-[amino-hydroxyalkanoyl] aminogycoside antibiotics (columns 1-2).

Claims 54-67 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakagawa et al (Microbial Drug Resistance,), Nakagawa et al (J. of Antibiotics, Shechter et al, Umezawa et al or Cron et al) as applied to claims 38-54, 63-67 and 72 above, and further in view of Hendricks et al (U.S. Patent No. 5,699,789) or Speirs et al (U.S. Patent no. 6,890,907).

Each of Nakagawa et al, Shechter et al, Umezawa et al and Cron et al discloses aminoglycosides derivatives having antibacterial activity. To combine said antibacterial compounds with other antibacterial compounds would have been prima facie obvious to a person having ordinary skill in the art at the time the claimed invention was made because such a person would have expected the resulting composition to possess antibacterial activity. Further, administration of aminoglycosides using inhaler was well known inn the art at the time the claimed invention was made as disclosed by Hendricks et al (column 6, lines 46-50) and Speirs et al. Therefore, it would have been prima facie obvious to a person having ordinary skill in the art at the time the claimed invention was made to administer the aminoglycoside antibiotics disclosed by each of Nakagawa et al, Shechter et al, Umezawa et al and Cron et al by inhalation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elli Peselev whose telephone number is (571) 272-0659. The examiner can normally be reached on 8.00-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elli Peselev

ELLI PESELEV
PRIMARY EXAMINER
GROUP 1200